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THE CHILDREN'S HOSPITAL,
CINCINNATI 29, OHIO.
ELLAND AND BETHESDA AVES.

February 28,1948

Dr. Michael Heidelberger
Department of Biochemistry
College of Physicians and Surgeons
Columbia-Presbyterian Medical Center
New York,New York

Dear Dr. Heidelberger:

After eight months here at the Cincinnati Children's Hospital during all of which time I have kept planning to write to you, I have finally brought contemplations to reality. The last six months of my pediatric training at Babies Hospital were a bewildering mass of clinical-duties which so interfered with the research project you had so kindly permitted me to start that the project was never completed. Ever since leaving New York I have felt that I never justified the time and attention you gave to me, and the unfinished problem still haunts me.

During my last months there I tried to interest others in the matter inorder that it be further pursued. Dr. Fieschel(spelling???) was very interested and I gave him sera on several cases, but he indicated that it might be years before he got to complement determinations.

I had not written up the work completely because it remained in preliminary stages. Over 100 determinations were done, some 100 or so of which were technically satisfactory. I do not feel justified in drawing any definite conclusions from the work, but again state that it indicated that "normal" sera ranged from 25-45 units in the vast majority of cases. Variation was such that no age,sex, or race factor was detectable.

Bearing out the suspicion which prompted the study, all four cases of Acute Glomerulonephritis revealed low complement levels and the two cases studied early in the disease revealed levels far below any of the controls(14.2 in one 3 weeks after onset and 15.7units in another one week after onset). The low complement level gradually rose, but even after one month was only in the very lowest range of"normal"

Chronic nephritis studied in several cases revealed "normal"-range levels. Many streptococcus adenitis and pharyngitis cases revealed no significant complement drop,even in convalescence. Rheumatic fever often gave normal levels, but a few active cases gave levels lower than any of the "normals" and this matter demanded much further investigation. Nephrosis gave normal levels in one old case and other cases results were confused by lipemic sera.

This, then, again summarizes the major findings. None of the findings were significantly conclusive to warrant publication, I felt, but I thought that an extensive study carried out along the very same lines might yield valuable material. Rate of regeneration of complement in nephritis and serum reactions could be studied. Study for determination of which component was reduced the most was certainly indicated. Study of anticomplementary activity of lipemic sera in nephrosis was needed.

I fully realized the need for this work and the improtance of doing it, yet I was committed to my clinical responsibilities and it remained unfinished.

I write now to inquire whether you have been able to further pursue this work with human sera. I hope someone has been found to continue it in as thorough a study as it warrants. I further want to request that If there is anyone interested in the problem you let me know inorder that I may send further sera for study. I should be very pleased to be able to send sera on nephritic patients collected serially during their illness to you if you thought complement levels could be determined on them by someone in your laboratory. We have much more nephritis here than I saw at Babies Hospital and the oportunity of obtaining serial sera is excellent. It is such that I could not resist drawing sera on four cases of nephritis I found on the wards.

If there is any chance that you could have complement levels determined, I should like to mail these sera to you. In them alone should be valuable material, for they are all cases of acute glomerulonephritis,all near enough to the onset to show some complement depression if the observation is valid.

Since ideal cases for such a study are numerous and readily available to me now(I cover services at both the 350 bed Children's Hospital and at the larger Cincinnati General Hospital) I would be very pleased if you could make use of serial sera from well selected cases - perhaps with interspersed controls of the same age.

The observation of low complement in many diseases-including nephritis -appears in the literature, but no extensive studies of this matter have come to my attention. Aside from the theoretical importance of such studies, the value of complement determination in suspected glomerulonephritis might be important (perhaps also in distinguishing acute from chronic nephritis).

I wish that I might help in further laboratory work on this problem, but, as I outlined to you, I have committed myself to a fairly long-term program. After completing my year here in June - bringing my pediatric training to 27 months - I shall head for California Institute of Technology where I shall work in the Physical Chemistry Department. There I shall work mostly -at first,at least - with Dr. John Kirkwood, the physical chemist formerly of Cornell - on new methods of electrophoretic study of proteins. After improving my background in physics and chemistry I hope to launch into work on nucleoproteins of viruses and genes in which my greatest interest lies.

I am sorry that I did not find the oportunity to express my deep gratitude to you for your interest in my problem and the great encouragement you gave me. The fault that it was not completed lay wholly with me and my clinical duties. I shall always remember your generous attention & provision of laboratory fascilities, and shall always regret that I was unable to present you with a more finished piece of investigative endeavour. If I can still contribute to the study of the problem,however, by obtaining serial samples of nephritic sera to be shipped frozen to you by air-express, I should be most happy, for I feal guilty of not having seen that this work - which I still consider very important - has not been brought to completion.

If you can use the sera I shall promptly send a few fresh,frozen nephritic sera with clinical data on the cases to you and welcome the opportunity to continue collecting sera both here and in California.

Respectfully yours,

D. Carleton Gajdusek, M.D.

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